Servier Presents Transformational Data from Pivotal Phase 3 INDIGO Trial of Vorasidenib in Recurrent or Residual Grade 2 IDH-Mutant Diffuse Glioma

Vorasidenib demonstrated an unprecedented improvement in progression free survival with a median of 27.7 months in patients with residual or recurrent grade 2 glioma with an IDH1/2 mutation; key secondary endpoint of time to next intervention significantly improved in the vorasidenib arm

Results presented at the ASCO 2023 plenary session, highlighting significance for patients with IDH-mutant diffuse glioma

Results of the INDIGO study have been simultaneously published in the New England Journal of Medicine

BOSTON, June 5, 2023 – Servier, a leader in oncology committed to bringing innovative therapies to the patients we serve, today presented results from the pivotal Phase 3 INDIGO clinical trial investigating vorasidenib, an investigational, oral, selective, highly brain-penetrant dual inhibitor of mutant IDH1/2 enzymes in patients with residual or recurrent isocitrate dehydrogenase 1 or 2 (IDH1/2) mutant low-grade glioma who have been treated with surgery only. INDIGO succeeded in meeting its primary endpoint of progression free survival (PFS) per blinded independent review committee (BIRC) and key secondary endpoint of time to next intervention (TTNI) at the prespecified second interim analysis. The data were presented as a late breaking abstract during the plenary session at the 2023 Annual Meeting of the American Society of Clinical Oncology (ASCO), and simultaneously published in the New England Journal of Medicine.

The primary endpoint, PFS per BIRC, was statistically significant and clinically meaningful in favor of the vorasidenib arm (HR, 0.39; 95% CI, 0.27 to 0.56; 1-sided P=0.000000067), median PFS for vorasidenib and placebo was 27.7 vs 11.1 months, respectively. TTNI was also statistically significant (HR, 0.26; 95% CI, 0.15 to 0.43; 1-sided P=0.000000019). Median TTNI was not reached for vorasidenib and 17.8 months for placebo.

“Grade 2 gliomas are progressive, malignant brain tumors with a poor prognosis, and the current treatment paradigm, which can be associated with short- and long-term toxicities, has not seen progress in more than two decades,” said Ingo K. Mellinghoff, M.D., Chair, Department of Neurology, Memorial Sloan Kettering Cancer Center. “For patients living with IDH mutant low-grade glioma, as determined by molecular testing, treatment with a targeted therapy such as vorasidenib has the potential to provide transformative benefits.”

“The overwhelmingly positive INDIGO results convincingly demonstrate the impact of targeting IDH mutations early in cancer biology where a monotherapy approach can lead to a profoundly meaningful outcome for patients with recurrent or residual IDH-mutant grade 2 gliomas,” said Susan Pandya,

M.D., Head of Cancer Metabolism Global Development Oncology & Immuno-Oncology, Servier Pharmaceuticals. “IDH mutations are disease defining alterations in IDH-mutant diffuse gliomas and these pivotal data coupled with vorasidenib’s especially high penetration of the blood-brain barrier, offer opportunities to evolve the treatment landscape for patients living with this malignancy. We look forward to working with the FDA on its review of vorasidenib as a potential therapy in IDH-mutant diffuse glioma.”

INDIGO is a registration-enabling Phase 3 global, randomized, double-blinded placebo-controlled study of vorasidenib in patients with residual or recurrent grade 2 glioma with an isocitrate dehydrogenase 1/2 (IDH1/2) mutation who have undergone surgery as their only treatment. IDH1/2 mutations occur in approximately 80% and 4% of grade 2 gliomas, respectively.

As of September 6, 2022 (2nd planned interim analysis data cutoff), 331 patients were randomized globally to receive vorasidenib (n=168) 40 mg daily or placebo (n=163) continuously in 28-day cycles. Of the 331 patients, 172 had oligodendroglioma (88 vorasidenib; 84 placebo) and 159 patients had astrocytoma (80 vorasidenib; 79 placebo). Median time from the last surgery until randomization was 2.5 years on the vorasidenib arm vs 2.2 years on the placebo arm.

The safety profile for vorasidenib was well tolerated and consistent with Phase 1 results. The most common Grade ≥3 adverse events for patients receiving vorasidenib vs placebo were alanine aminotransferase increased (9.6% vs 0), aspartate aminotransferase increased (4.2% vs 0) and seizure (4.2% vs 2.5%).

Vorasidenib was granted fast track designation by the U.S. Food & Drug Administration (FDA) in March 2023. Servier is working to determine timelines for submission of a New Drug Application (NDA) for vorasidenib to the FDA.

“Patients with brain cancer live with the constant fear of what their future looks like. For over twenty years, the lack of new treatment options has put patients in a position of making the difficult decision to accept a treatment that has significant side effects or to preserve cognitive function for as long as possible”, said Brock Greene, Founder of Oligo Nation, a leading brain cancer patient organization. “Servier’s positive clinical trial data for a targeted therapy in IDH-mutant glioma that may possibly improve outcomes for patients provides this community with new hope that they have been waiting decades for.

About the INDIGO Phase 3 Trial

INDIGO is a registration-enabling Phase 3 global, randomized, double-blinded placebo-controlled study of vorasidenib in patients with residual or recurrent grade 2 glioma with an isocitrate dehydrogenase 1/2 (IDH1/2) mutation who have undergone surgery as their only treatment. (NCT04164901).

About Glioma[1]

Gliomas are tumors that arise from glial or precursor cells within the central nervous system (CNS). The 2021 WHO classification recognizes four general groups of gliomas, one of which is adult-type diffuse gliomas. These diffuse gliomas are the most common primary malignant brain tumors in adults. The pathogenesis and prognosis of these tumors are tightly linked to mutations (or lack thereof) in the metabolic enzyme isocitrate dehydrogenase (IDH), and molecular testing is required for proper diagnosis. As of 2021, adult-type diffuse gliomas are sub-divided into only three categories:

- Astrocytoma, IDH-mutant (CNS WHO grades 2-4)
- Oligodendroglioma, IDH-mutant and1p19q-codeleted (CNS WHO grades 2-3)

- Glioblastoma, IDH-wildtype (CNS WHO grade 4)

[1] Neuro Oncology. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. https://academic.oup.com/neuro-oncology/article/23/8/1231/6311214 Last accessed-3.28.23

Press contacts

presse@servier.com

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To promote access to quality care for all at a lower cost, the Group also offers a range of quality generic drugs covering most pathologies, relying on strong brands in France, Eastern Europe, Brazil and Nigeria.

In all these areas, the Group includes the patient voice at each stage of the life cycle of a medicine.

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